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TITLE: LIMITED TOXICITY AND MUTAGENICITY TESTING OF FIVE UNICHARGE PROPELLANT COMPOUNDS

SUBTITLE: Evaluation of Two Unicharge Propellants in the Acute Oral Toxicity Study in Mice (14 Day)

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CONTRACTING ORGANIZATION: Pharmakon Research International, Inc.
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13. ABSTRACT *(Maximum 200 words)*

Bis-(2,2-dinitropropyl) acetal/formal (~50/50 mixture) ± diphenyl amine stabilizer (BDNPA/F±DPA) were tested for oral toxicity. Groups of ten mice per dose level were fasted and administered the test article orally by gavage. Animals were observed for clinical signs and mortality at 1 and 4 hours after dosing and once daily for 14 days. Based upon the results from the Acute Oral Toxicity Study in Mice (14 Day), the definitive acute oral LD_{50} (combined sexes) for BDNPA/F+DPA was determined to be 2601.9 mg/kg with 95% confidence limits of 1814.0 to 3732.1 mg/kg. The definitive acute oral LD_{50} (combined sexes) for BDNPA/F-DPA was determined to be 3764.2 mg/kg with 95% confidence limits of 3081.4 to 4598.3 mg/kg.

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Oral Toxicity, Unicharge, Propellants, bis(2,2-dinitropropyl) acetal, bis-(2,2-dinitropropyl) formal, lab animals, RA III

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TABLE OF CONTENTS

Evaluation of Two Unicharge Propellants in the Acute Oral Toxicity Study in Mice (14 Day)

EXECUTIVE SUMMARY

In dose-range-finding studies, test articles bis-(2,2-dinitropropyl) acetal with diphenyl amine stabilizer and bis-(2,2-dinitropropyl) formal without diphenyl amine stablizer were orally administered to three groups of two mice (one/sex/group) per study at dose levels of 500, 2500 and 5000 mg/kg. Signs observed in both treatment groups included decreased activity, abnormal stance, abnormal gait, dyspnea and prostration. None of the mice died at 500 mg/kg, two of two died at 2500 and 5000 mg/kg in the bis-(2,2-dinitropropyl) acetal with diphenyl amine stabilizer treated animals. Of the animals that received bis-(2,2-dinitropropyl) formal without diphenyl amine stablizer, none of the mice died at 500 mg/kg, one of two died at 2500 mg/kg and two of two died at 5000 mg/kg. Based upon these results Definitive LD_{50}s were performed.

In a Definitive LD_{50}, bis-(2,2-dinitropropyl) acetal with diphenyl amine stabilizer was orally administered to five groups of ten mice (five males and five females per group), at dose levels of 500, 1000, 1600, 3200 and 5000 mg/kg. Signs observed included decreased activity, abnormal gait, abnormal stance, dyspnea and prostration. There was an apparent increase in mean body weight in all surviving animals during the study. None of the mice died at 500 mg/kg. Two of ten mice died at both 1000 and 1600 mg/kg. Four of ten animals died at 3200 mg/kg and nine of ten animals died at 5000 mg/kg. Necropsy of the animals that died on study revealed fluid-filled and/or distended intestines. No visible lesions were observed in any animal at terminal necropsy.

In a Definitive LD_{50}, bis-(2,2-dinitropropyl) formal without diphenyl amine stablizer was orally administered to five groups of ten mice (five males and five females per group) at dose levels of 1000, 1600, 2500, 4000 and 5000 mg/kg. Signs observed included decreased activity, abnormal stance, abnormal gait, dyspnea and prostration. There was an apparent increase in mean body weight in all surviving animals during the study. None of the animals died at 1600 mg/kg. Two of ten animals died at 1000 and 2500 mg/kg. Three of ten animals died at 4000 mg/kg and nine of ten died at 5000 mg/kg. Necropsy of the animals that died on study revealed distended and/or fluid-filled intestines. No visible lesions were observed in any of the animals at terminal necropsy.

Based upon these results from the Acute Oral Toxicity Study in Mice (14 Day), the definitive acute oral LD_{50} (combined sexes) for bis-(2,2-dinitropropyl) acetal with diphenyl amine stabilizer was determined to be 2601.9 mg/kg with 95% confidence limits of 1814.0 to 3732.1 mg/kg. The LD_{50} for males was determined to be 2264.7 mg/kg with 95% confidence limits of 1244.6 to 4121.2 mg/kg. The data generated to determine the LD_{50} for females did not lend itself to the statistical method employed. The definitive acute oral LD_{50} (combined sexes) for bis-(2,2-dinitropropyl) formal without diphenyl amine stablizer was determined to be 3764.2 mg/kg with 95% confidence limits of

Evaluation of Two Unicharge Propellants in the Acute Oral Toxicity Study in Mice (14 Day)

EXECUTIVE SUMMARY

3081.4 to 4598.3 mg/kg. The LD_{50} for males was determined to be 4323.4 mg/kg with 95% confidence limits of 3328.04 to 5616.5 mg/kg. The LD_{50} for females was determined to be 3566.2 mg/kg with 95% confidence limits of 1648.3 to 7715.4 mg/kg.

Evaluation of Two Unicharge Propellants in the Acute Oral Toxicity Study in Mice (14 Day)

PH 403-US-001,002-91

STUDY DESCRIPTION

Sponsor:	U.S. Army Medical Research and Development Laboratory Fort Detrick Frederick, MD 21702-5010
Testing Facility:	Pharmakon Research International, Inc. P.O. Box 609 Waverly, PA 18471
Test Facility S.O.P. No.:	PH-403
Study No.:	PH 403-US-001-91 PH 403-US-002-91
Purpose of the Study:	To determine the acute oral median lethal dose (LD_{50}) of the test article in mice.
Ownership of the Study:	The sponsor owns the study. All raw data, analysis and reports are the property of the sponsor.
Study Monitor:	Major Nathaniel Powell, U.S. Army Medical Research and Development Laboratory
Study Director:	Victor T. Mallory, B.S., RLAT, Pharmakon Research International, Inc.
Technical Performance:	Thomas O'Neill, B.S., LAT, Kim DiLeo, B.S., LAT, Maura J. Bieszczad and Shirley Chappuis, A.S., AVT, LAT
Q.A.U. Responsible Personnel:	Leslie J. Pinnell, M.S.
Date Study Director Signed Protocols:	September 23, 1991
Dates of Technical Performance:	Dose-Range-Finding **PH 403-US-001-91** - October 21, 1991 through October 24, 1991 **PH 403-US-002-91** - October 21, 1991 through October 24, 1991

Evaluation of Two Unicharge Propellants in the Acute Oral Toxicity Study in Mice (14 Day)
PH 403-US-001,002-91

Definitive LD_{50}
PH 403-US-001-91 - October 30, 1991 through November 29, 1991

PH 403-US-002-91 - October 30, 1991 through November 26, 1991

Good Laboratory Practice Statement: These studies were conducted in compliance with the Good Laboratory Practice Regulations. There were no deviations from the GLP Regulations which affected the quality or integrity of the study. Q.A.U. findings from the inspections conducted of this study and from the audit of the final report are documented and have been provided to the study director and the test facility management.

Records Maintained: All raw data, final reports, documentation and protocol will be maintained in the archives of Pharmakon Research International, Inc.

Recordings: Standard Pharmakon Notebook

Statistics: Statistics were calculated using Systat, Version 4.1, by Systat, Inc., Evanston, IL. LD_{50} determinations were calculated by the method of Litchfield and Wilcoxon via the Pharmacological Calculation System, Version 4.1.

Notebook Reference: Notebook #1539, pages 80-82, 84-95, 132-134, 136-147,

TEST ARTICLES

TEST ARTICLE	DESCRIPTION	LOT #	CAS #	DATE SUBMITTED
bis-(2,2-dinitropropyl) acetal with diphenyl amine stabilizer (BDNPA/F+DPA)	yellow liquid	Set #1	5108-69-0	9/19/91
bis-(2-2-dinitropropyl) formal without diphenyl amine stabilizer (BDNPA/F-DPA)	yellow liquid	Set #2	5917-61-3	9/19/91

Analysis of Purity: The purity, identity, strength and stability of the test articles were the responsibility of the sponsor.

Evaluation of Two Unicharge Propellants in the Acute Oral Toxicity Study in Mice (14 Day)
PH 403-US-001,002-91

Stability:	There was no apparent change in the physical appearance of the test articles during administration.

TEST SYSTEM

Species:	Mouse
Strain:	CD-1
Supplier (Source):	Charles River Laboratories, Inc., Wilmington, Massachusetts
Sex:	Male and female
Age at Initiation:	8-10 weeks
Weight Range:	Dose-Range-Finding - 20-25 grams Definitive LD_{50} - 18-25 grams
No. on Study:	Ten (10) (five males and five females) per group.
Method and Justification for Randomization:	Selection of mice based upon body weight
Acclimation Period:	Minimum of five (5) days
System of Identification:	Cage cards were marked with the study number, animal number, dose level and sex. Mice were ear tagged.

HUSBANDRY

Research Facility Registration:	U.S.D.A. Registration No. 23-R-107 under the Animal Welfare Act 74: SC 2131 et seq.
Animal Rooms:	Separate isolation by test system. Light cycle - 12 hours light, 12 hours dark. Temperature/Relative Humidity - Every attempt was made to maintain a temperature of 22° ± 3°C (66° - 77°F) and a relative humidity of 30 to 70%. Any excursions outside the temperature or humidity ranges were of small magnitude and/or brief duration and did not adversely affect the validity of the study.

Evaluation of Two Unicharge Propellants in the Acute Oral Toxicity Study in Mice (14 Day)
PH 403-US-001,002-91

Housing:	Mice were housed individually in stainless steel ½" wire mesh cages, sized in accordance with the "Guide for the Care and Use of Laboratory Animals" of the Institute of Laboratory Animal Resources, National Research Council.
Sanitization:	Waste material was removed twice weekly. Cages and feeders were sanitized every two weeks.
Food:	Wayne Teklad Blox^{R}, ad libitum. Food was checked daily and added or replaced as needed. Feeders are designed to reduce soiling, bridging and scattering.
Food Analysis:	There were no contaminants that were reasonably expected to be present in the dietary material known to be capable of interfering with the purpose or conduct of the study.
Water:	Fresh tap water, ad libitum.
Water Analysis:	Water is monitored for contaminants at periodic intervals according to Standard Operating Procedure PH-018.

METHODS

Rationale for Test System:	As required by the regulatory agencies.
Compound Preparation:	All test articles were dosed as received from the sponsor using specific gravity (1.392 gm/mL) conversion.
Dose Administration:	Bis-(2,2-dinitropropyl) acetal with diphenyl amine stabilizer - 500, 1000, 1600, 3200 and 5000 mg/kg Bis-(2,2-dinitropropyl) formal without diphenyl amine stablizer - 1000, 1600, 2500, 4000 and 5000 mg/kg
Rationale for Dose Selection:	Based upon the results of a dose-range -finding study.
Route of Administration:	The test articles were administered in a single dose by gavage using a stainless steel gavage needle.

Evaluation of Two Unicharge Propellants in the Acute Oral Toxicity Study in Mice (14 Day)
PH 403-US-001,002-91

Rationale for Route of Administration:	According to the EPA Federal Register, Vol. 50, No. 188, Friday, September 27, 1985 and the Organization for Economic Co-operation and Development (OECD) Guidelines for Testing Chemicals, ISBN 92-64-12221-4, adopted by the council at the 535th meeting on May 12, 1981.
Frequency and Duration of Administration:	Once (1) per test article
No. of Animals Per Dose Group:	Ten (10)
Length of Study:	Fourteen (14) days
Method of Study Performance:	Dose-Range-Finding Study In dose-range-finding studies, three groups of two mice (one male and one female per group) per study were fasted and administered neet material, at dose levels of 500, 2500 and 5000 mg/kg, orally by gavage. The mice were observed at approximately 1, 4, 24, 48 and 72 hours after dosing for pharmacological and toxicological effects and mortality. Definitive LD_{50} In Definitive LD_{50}s, groups of ten mice (five males and five females per group) were fasted and administered neet material, at dose levels 500, 1000, 1600, 3200 and 5000 mg/kg [bis-(2,2-dinitropropyl) acetal with diphenyl amine stabilizer] and 1000, 1600, 2500, 4000 and 5000 mg/kg [bis-(2,2-dinitropropyl) formal without diphenyl amine stablizer], orally by gavage. The mice were observed at approximately 1, 4 and 24 hours after dosing and once daily through Day 14 for pharmacological and toxicological effects. Viability was checked daily. Body weights were recorded at study initiation and Day 14 or when found dead. All surviving mice were sacrificed by CO_2 inhalation and a gross necropsy performed.

RESULTS

Dose-Range-Finding Study
Signs observed in both treatment groups included decreased activity, abnormal stance, abnormal gait, dyspnea and prostration. None of the mice died at 500 mg/kg and two of two died at 2500 and 5000 mg/kg in the bis-(2,2-dinitropropyl) acetal with diphenyl amine

stabilizer treated animals. Of the animals that received bis-(2,2-dinitropropyl) formal without diphenyl amine stablizer, none of the mice died at 500 mg/kg, one of two died at 2500 mg/kg and two of two died at 5000 mg/kg. Based upon these results Definitive LD_{50}s were performed.

Definitive LD_{50}

Signs observed in the animals receiving bis-(2,2-dinitropropyl) acetal with diphenyl amine stabilizer included decreased activity, abnormal gait, abnormal stance, dyspnea and prostration. There was an apparent increase in mean body weight in all surviving animals during the study. None of the mice died at 500 mg/kg. Two of ten mice died at both 1000 and 1600 mg/kg. Four of ten animals died at 3200 mg/kg and nine of ten animals died at 5000 mg/kg. Necropsy of the animals that died on study revealed fluid-filled and/or distended intestines. No visible lesions were observed in any animal at terminal necropsy.

Signs observed in the animals receiving bis-(2,2-dinitropropyl) formal without diphenyl amine stablizer included decreased activity, abnormal stance, abnormal gait, dyspnea and prostration. There was an apparent increase in mean body weight in all surviving animals during the study. None of the animals died at 1600 mg/kg. Two of ten animals died at 1000 and 2500 mg/kg. Three of ten animals died at 4000 mg/kg and and nine of ten died at 5000 mg/kg. Necropsy of the animals that died on study revealed distended and/or fluid-filled intestines. No visible lesions were observed in any of the animals at terminal necropsy.

CONCLUSIONS

Based upon these results from the Acute Oral Toxicity Study in Mice (14 Day), the definitive acute oral LD_{50} (combined sexes) for bis-(2,2-dinitropropyl) acetal with diphenyl amine stabilizer was determined to be 2601.9 mg/kg with 95% confidence limits of 1814.0 to 3732.1 mg/kg. The LD_{50} for males was determined to be 2264.7 mg/kg with 95% confidence limits of 1244.6 to 4121.2 mg/kg. The data generated to determine the LD_{50} for females did not lend itself to the

statistical method employed. The definitive acute oral LD_{50} (combined sexes) for bis-(2,2-dinitropropyl) formal without diphenyl amine stablizer was determined to be 3764.2 mg/kg with 95% confidence limits of 3081.4 to 4598.3 mg/kg. The LD_{50} for males was determined to be 4323.4 mg/kg with 95% confidence limits of 3328.04 to 5616.5 mg/kg. The LD_{50} for females was determined to be 3566.2 mg/kg with 95% confidence limits of 1648.3 to 7715.4 mg/kg.

Table I

Summary of Clinical Observations of Two Unicharge Propellants in the Acute Exposure Oral Toxicity Study in Mice (14 Day)

PH 403-US-001,002-91

Bis-(2,2-Dinitropropyl) Acetal with Diphenyl Amine Stabilizer

@ 500 mg/kg

Clinical Signs	Sex	Hours		Days												
		1	24	2	3	4	5	6	7	8	9	10	11	12	13	14
No signs	M	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
	F	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5

1000 mg/kg

Clinical Signs	Sex	Hours			Days													
		1	4	24	2	3	4	5	6	7	8	9	10	11	12	13	14
No signs	M	5	3	3	4	4	4	4	4	4	4	4	4	4	4	4	4
	F	5	4	2	4	4	4	4	4	4	4	4	4	4	4	4	4
Decreased Activity	M	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
	F	0	1	2	0	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal Gait	M	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	F	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal Stance	M	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	F	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
Dyspnea	M	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	F	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0

Table I (continued)

Summary of Clinical Observations of Two Unicharge Propellants
in the Acute Exposure Oral Toxicity Study in Mice (14 Day)

PH 403-US-001,002-91

Bis-(2,2-Dinitropropyl) Acetal with Diphenyl Amine Stabilizer

@ 1600 mg/kg

Clinical Signs	Sex	Hours			Days												
		1	4	24	2	3	4	5	6	7	8	9	10	11	12	13	14
No signs	M	5	3	3	3	3	3	4	4	4	4	4	4	4	4	4	4
	F	5	2	1	1	1	1	4	4	4	4	4	4	4	4	4	4
Decreased Activity	M	0	2	2	1	1	1	0	0	0	0	0	0	0	0	0	0
	F	0	3	3	3	3	3	0	0	0	0	0	0	0	0	0	0
Abnormal Gait	M	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
	F	0	0	2	2	2	2	0	0	0	0	0	0	0	0	0	0
Abnormal Stance	M	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
	F	0	0	2	2	2	2	0	0	0	0	0	0	0	0	0	0
Dyspnea	M	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
	F	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0

Table I (continued)

Summary of Clinical Observations of Two Unicharge Propellants
in the Acute Exposure Oral Toxicity Study in Mice (14 Day)

PH 403-US-001,002-91

Bis-(2,2-Dinitropropyl) Acetal with Diphenyl Amine Stabilizer

@ 3200 mg/kg

Clinical Signs	Sex	Hours			Days												
		1	4	24	2	3	4	5	6	7	8	9	10	11	12	13	14
No signs	M	5	0	0	1	1	2	2	2	2	2	2	2	2	2	2	2
	F	5	0	0	4	4	4	4	4	4	4	4	4	4	4	4	4
Decreased Activity	M	0	3	2	1	1	0	0	0	0	0	0	0	0	0	0	0
	F	0	5	5	1	1	0	0	0	0	0	0	0	0	0	0	0
Abnormal Gait	M	0	2	1	1	0	0	0	0	0	0	0	0	0	0	0	0
	F	0	3	3	1	1	0	0	0	0	0	0	0	0	0	0	0
Abnormal Stance	M	0	2	1	1	0	0	0	0	0	0	0	0	0	0	0	0
	F	0	3	3	1	1	0	0	0	0	0	0	0	0	0	0	0
Dyspnea	M	0	2	1	1	0	0	0	0	0	0	0	0	0	0	0	0
	F	0	3	3	1	1	0	0	0	0	0	0	0	0	0	0	0

Table I (continued)

Summary of Clinical Observations of Two Unicharge Propellants
in the Acute Exposure Oral Toxicity Study in Mice (14 Day)

PH 403-US-001,002-91

Bis-(2,2-Dinitropropyl) Acetal with Diphenyl Amine Stabilizer

@ 5000 mg/kg

Clinical Signs	Sex	Hours			Days												
		1	4	24	2	3	4	5	6	7	8	9	10	11	12	13	14
No signs	M	5	0	0	-	-	-	-	-	-	-	-	-	-	-	-	-
	F	5	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1
Decreased Activity	M	0	5	3	-	-	-	-	-	-	-	-	-	-	-	-	-
	F	0	5	1	1	1	1	0	0	0	0	0	0	0	0	0	0
Abnormal Gait	M	0	3	3	-	-	-	-	-	-	-	-	-	-	-	-	-
	F	0	4	1	1	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal Stance	M	0	3	3	-	-	-	-	-	-	-	-	-	-	-	-	-
	F	0	4	1	1	0	0	0	0	0	0	0	0	0	0	0	0
Dyspnea	M	0	3	3	-	-	-	-	-	-	-	-	-	-	-	-	-
	F	0	4	1	1	0	0	0	0	0	0	0	0	0	0	0	0
Prostration	M	0	0	0	-	-	-	-	-	-	-	-	-	-	-	-	-
	F	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0

-: Denotes all animals died on study

Table I (continued)

Summary of Clinical Observations of Two Unicharge Propellants
in the Acute Exposure Oral Toxicity Study in Mice (14 Day)

PH 403-US-001,002-91

Bis-(2,2-Dinitropropyl) Formal without Diphenyl Amine Stablizer

@ 1000 mg/kg

Clinical Signs	Sex	Hours			Days												
		1	4	24	2	3	4	5	6	7	8	9	10	11	12	13	14
No signs	M	5	5	5	4	4	4	5	5	5	5	5	5	5	5	5	5
	F	5	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3
Decreased Activity	M	0	0	0	1	1	1	0	0	0	0	0	0	0	0	0	0
	F	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

@ 1600 mg/kg

Clinical Signs	Sex	Hours			Days												
		1	4	24	2	3	4	5	6	7	8	9	10	11	12	13	14
No signs	M	5	2	3	3	3	3	5	5	5	5	5	5	5	5	5	5
	F	5	3	3	3	3	3	5	5	5	5	5	5	5	5	5	5
Decreased Activity	M	0	3	2	2	2	2	0	0	0	0	0	0	0	0	0	0
	F	0	2	2	2	2	2	0	0	0	0	0	0	0	0	0	0

Table I (continued)

Summary of Clinical Observations of Two Unicharge Propellants
in the Acute Exposure Oral Toxicity Study in Mice (14 Day)

PH 403-US-001,002-91

Bis-(2,2-Dinitropropyl) Formal without Diphenyl Amine Stablizer

@ 2500 mg/kg

Clinical Signs	Sex	Hours			Days												
		1	4	24	2	3	4	5	6	7	8	9	10	11	12	13	14
No signs	M	5	1	2	2	2	2	5	5	5	5	5	5	5	5	5	5
	F	5	1	2	2	2	2	3	3	3	3	3	3	3	3	3	3
Decreased Activity	M	0	4	3	3	3	3	0	0	0	0	0	0	0	0	0	0
	F	0	4	3	2	1	1	0	0	0	0	0	0	0	0	0	0
Abnormal Gait	M	0	0	1	1	1	1	0	0	0	0	0	0	0	0	0	0
	F	0	1	1	2	1	1	0	0	0	0	0	0	0	0	0	0
Abnormal Stance	M	0	0	1	1	1	1	0	0	0	0	0	0	0	0	0	0
	F	0	1	1	2	1	1	0	0	0	0	0	0	0	0	0	0
Dyspnea	M	0	0	1	1	1	1	0	0	0	0	0	0	0	0	0	0
	F	0	1	1	2	1	1	0	0	0	0	0	0	0	0	0	0

Table I (continued)

Summary of Clinical Observations of Two Unicharge Propellants
in the Acute Exposure Oral Toxicity Study in Mice (14 Day)

PH 403-US-001,002-91

Bis-(2,2-Dinitropropyl) Formal without Diphenyl Amine Stablizer

@ 4000 mg/kg

Clinical Signs	Sex	Hours			Days												
		1	4	24	2	3	4	5	6	7	8	9	10	11	12	13	14
No signs	M	5	0	0	2	2	3	3	3	3	3	3	3	3	3	3	3
	F	5	0	0	4	4	4	4	4	4	4	4	4	4	4	4	4
Decreased Activity	M	0	3	3	1	1	0	0	0	0	0	0	0	0	0	0	0
	F	0	4	4	0	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal Gait	M	0	3	2	1	0	0	0	0	0	0	0	0	0	0	0	0
	F	0	4	3	0	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal Stance	M	0	3	2	1	0	0	0	0	0	0	0	0	0	0	0	0
	F	0	4	3	0	0	0	0	0	0	0	0	0	0	0	0	0

Table I (continued)

Summary of Clinical Observations of Two Unicharge Propellants
in the Acute Exposure Oral Toxicity Study in Mice (14 Day)

PH 403-US-001,002-91

Bis-(2,2-Dinitropropyl) Formal without Diphenyl Amine Stablizer

@ 5000 mg/kg

Clinical Signs	Sex	Hours			Days												
		1	4	24	2	3	4	5	6	7	8	9	10	11	12	13	14
No signs	M	5	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1
	F	5	0	0	0	-	-	-	-	-	-	-	-	-	-	-	-
Decreased Activity	M	0	2	1	1	1	1	1	1	0	0	0	0	0	0	0	0
	F	0	3	2	0	-	-	-	-	-	-	-	-	-	-	-	-
Abnormal Gait	M	0	2	1	1	0	0	0	0	0	0	0	0	0	0	0	0
	F	0	3	1	0	-	-	-	-	-	-	-	-	-	-	-	-
Abnormal Stance	M	0	2	1	1	0	0	0	0	0	0	0	0	0	0	0	0
	F	0	3	1	0	-	-	-	-	-	-	-	-	-	-	-	-
Prostration	M	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	F	0	0	0	1	-	-	-	-	-	-	-	-	-	-	-	-

-: Denotes all animals died on study

Table II

Summary of Mortality of Two Unicharge Propellants
in the Acute Exposure Oral Toxicity Study in Mice (14 Day)

PH 403-US-001,002-91

Bis-(2,2-Dinitropropyl) Acetal with Diphenyl Amine Stabilizer

Dose (mg/kg)	Sex	No. of Mice	Days														Total Mortality
			0[a]	1	2	3	4	5	6	7	8	9	10	11	12	13	14	
500	M	5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0/5
500	F	5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0/5
1000	M	5	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1/5
1000	F	5	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1/5
1600	M	5	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1/5
1600	F	5	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1/5
3200	M	5	2	1	0	0	0	0	0	0	0	0	0	0	0	0	0	3/5
3200	F	5	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	1/5
5000	M	5	0	2	3	-	-	-	-	-	-	-	-	-	-	-	-	5/5
5000	F	5	0	3	0	1	0	0	0	0	0	0	0	0	0	0	0	4/5

a: Includes 1 and 4 hour observation periods
-: Denotes all animals died on study

Table II (continued)

Summary of Mortality of Two Unicharge Propellants
in the Acute Exposure Oral Toxicity Study in Mice (14 Day)

PH 403-US-001,002-91

Bis-(2,2-Dinitropropyl) Formal without Diphenyl Amine Stablizer

Dose (mg/kg)	Sex	No. of Mice	Days															Total Mortality
			0[a]	1	2	3	4	5	6	7	8	9	10	11	12	13	14	
1000	M	5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0/5
1000	F	5	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2/5
1600	M	5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0/5
1600	F	5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0/5
2500	M	5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0/5
2500	F	5	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	2/5
4000	M	5	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2/5
4000	F	5	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1/5
5000	M	5	3	1	0	0	0	0	0	0	0	0	0	0	0	0	0	4/5
5000	F	5	2	1	1	1	-	-	-	-	-	-	-	-	-	-	-	5/5

a: Includes 1 and 4 hour observation periods
-: Denotes all animals died on study

Table III. Summary of Body Weights (g) of Two Unicharge Propellants in the Acute Exposure Oral Toxicity Study in Mice (14 Day)

PH 403-US-001,002-91

Bis-(2,2-Dinitropropyl) Acetal with Diphenyl Amine Stabilizer

500 mg/kg

Animal Number	Sex	Initial	Final
3201	M	20	31
3202	M	24	34
3203	M	22	35
3204	M	25	34
3205	M	25	35
$\bar{x}$		23.2	33.8
S.D.		2.17	1.64
N		5	5
3206	F	24	29
3207	F	18	28
3208	F	21	25
3209	F	22	28
3210	F	21	29
$\bar{x}$		21.2	27.8
S.D.		2.17	1.64
N		5	5

1000 mg/kg

Animal Number	Sex	Initial	Final
3211	M	25	-
3212	M	24	34
3213	M	25	35
3214	M	25	35
3215	M	21	36
$\bar{x}$		24.0	35.0
S.D.		1.73	0.82
N		5	4
3216	F	20	25
3217	F	20	29
3218	F	21	30
3219	F	23	28
3220	F	21	-
$\bar{x}$		21.0	28.0
S.D.		1.23	2.16
N		5	4

-: Denotes animal died on study

Table III. (cont'd) Summary of Body Weights (g) of Two Unicharge Propellants in the Acute Exposure Oral Toxicity Study in Mice (14 Day)

PH 403-US-001,002-91

Bis-(2,2-Dinitropropyl) Acetal with Diphenyl Amine Stabilizer

1600 mg/kg

Animal Number	Sex	Initial	Final
3221	M	23	-
3222	M	22	28
3223	M	24	33
3224	M	24	28
3225	M	25	36
$\bar{x}$		23.6	31.3
S.D.		1.14	3.95
N		5	4
3226	F	21	27
3227	F	21	26
3228	F	23	-
3229	F	20	30
3230	F	21	28
$\bar{x}$		21.2	27.8
S.D.		1.10	1.71
N		5	4

3200 mg/kg

Animal Number	Sex	Initial	Final
3171	M	23	30
3172	M	25	-
3173	M	23	-
3174	M	23	35
3175	M	25	-
$\bar{x}$		23.8	
S.D.		1.10	a
N		5	2
3176	F	22	27
3177	F	21	28
3178	F	22	27
3179	F	21	-
3180	F	20	25
$\bar{x}$		21.2	26.8
S.D.		0.84	1.26
N		5	4

-: Denotes animal died on study
a: Not applicable

Table III. (cont'd) Summary of Body Weights (g) of Two Unicharge Propellants in the Acute Exposure Oral Toxicity Study in Mice (14 Day)

PH 403-US-001,002-91

Bis-(2,2-Dinitropropyl) Acetal with Diphenyl Amine Stabilizer

5000 mg/kg

Animal Number	Sex	Initial	Final
3131	M	25	-
3132	M	24	-
3133	M	25	-
3134	M	24	-
3135	M	25	-
$\bar{x}$		24.6	a
S.D.		0.55	
N		5	0
3136	F	21	-
3137	F	20	-
3138	F	24	27
3139	F	20	-
3140	F	23	-
$\bar{x}$		21.6	a
S.D.		1.82	
N		5	1

-: Denotes animal died on study
a: Not applicable

Table III. (cont'd) Summary of Body Weights (g) of Two Unicharge Propellants in the Acute Exposure Oral Toxicity Study in Mice (14 Day)

PH 403-US-001,002-91

Bis-(2,2-Dinitropropyl) Formal without Diphenyl Amine Stablizer

1000 mg/kg

Animal Number	Sex	Initial	Final
3231	M	24	36
3232	M	25	32
3233	M	22	34
3234	M	21	28
3235	M	20	30
$\bar{x}$		22.4	32.0
S.D.		2.07	3.16
N		5	5
3236	F	22	26
3237	F	22	29
3238	F	25	-
3239	F	21	-
3240	F	21	28
$\bar{x}$		22.2	27.7
S.D.		1.64	1.53
N		5	3

1600 mg/kg

Animal Number	Sex	Initial	Final
3241	M	24	37
3242	M	25	31
3243	M	24	32
3244	M	23	33
3245	M	24	35
$\bar{x}$		24.0	33.6
S.D.		0.71	2.41
N		5	5
3246	F	20	28
3247	F	21	28
3248	F	20	30
3249	F	21	27
3250	F	21	29
$\bar{x}$		20.6	28.4
S.D.		0.55	1.14
N		5	5

-: Denotes animal died on study

Table III. (cont'd) Summary of Body Weights (g) of Two Unicharge Propellants in the Acute Exposure Oral Toxicity Study in Mice (14 Day)

PH 403-US-001,002-91

Bis-(2,2-Dinitropropyl) Formal without Diphenyl Amine Stablizer

2500 mg/kg

Animal Number	Sex	Initial	Final
3251	M	24	34
3252	M	23	29
3253	M	19	33
3254	M	21	29
3255	M	20	32
$\bar{x}$		21.4	31.4
S.D.		2.07	2.30
N		5	5
3256	F	20	28
3257	F	24	29
3258	F	20	-
3259	F	21	-
3260	F	21	28
$\bar{x}$		21.2	28.3
S.D.		1.64	0.58
N		5	3

4000 mg/kg

Animal Number	Sex	Initial	Final
3151	M	24	31
3152	M	23	-
3153	M	24	30
3154	M	24	37
3155	M	23	-
$\bar{x}$		23.6	32.7
S.D.		0.55	3.79
N		5	3
3156	F	22	24
3157	F	22	25
3158	F	21	-
3159	F	22	26
3160	F	22	26
$\bar{x}$		21.8	25.3
S.D.		0.45	0.96
N		5	4

-: Denotes animal died on study

Table III. (cont'd) Summary of Body Weights (g) of Two Unicharge Propellants in the Acute Exposure Oral Toxicity Study in Mice (14 Day)

PH 403-US-001,002-91

Bis-(2,2-Dinitropropyl) Formal without Diphenyl Amine Stablizer

5000 mg/kg

Animal Number	Sex	Initial	Final
3161	M	23	31
3162	M	24	-
3163	M	23	-
3164	M	24	-
3165	M	23	-
$\bar{x}$		23.4	a
S.D.		0.55	
N		5	1
3166	F	21	-
3167	F	21	-
3168	F	22	-
3169	F	22	-
3170	F	20	-
$\bar{x}$		21.2	a
S.D.		0.84	
N		5	0

-: Denotes animal died on study
a: Not applicable

Table IV

Necropsy Observations (Incidence Values) of Five Unicharge Propellants in the Acute Exposure Oral Toxicity Study in Mice (14 Day)

PH 403-US-001,002-91

Bis-(2,2-Dinitropropyl) Acetal with Diphenyl Amine Stabilizer

500 mg/kg

Observation	Interim Death Incidence		Terminal Necropsy Incidence	
	M	F	M	F
No visible lesions	-	0	5	5

1000 mg/kg

Observation	Interim Death Incidence		Terminal Necropsy Incidence	
	M	F	M	F
No visible lesions	1	0	4	4
Intestines distended	0	1	0	0

1600 mg/kg

Observation	Interim Death Incidence		Terminal Necropsy Incidence	
	M	F	M	F
No visible lesions	1	1	4	4

-: Not applicable

Table IV (continued)

Necropsy Observations (Incidence Values) of Five Unicharge Propellants in the Acute Exposure Oral Toxicity Study in Mice (14 Day)

PH 403-US-001,002-91

Bis-(2,2-Dinitropropyl) Acetal with Diphenyl Amine Stabilizer

3200 mg/kg

Observation	Interim Death Incidence		Terminal Necropsy Incidence	
	M	F	M	F
No visible lesions	3	0	2	4
Intestines fluid-filled red	0	1	0	0

5000 mg/kg

Observation	Interim Death Incidence		Terminal Necropsy Incidence	
	M	F	M	F
No visible lesions	5	4	-	1

-: Not applicable

Table IV (continued)

Necropsy Observations (Incidence Values) of Five Unicharge Propellants in the Acute Exposure Oral Toxicity Study in Mice (14 Day)

PH 403-US-001,002-91

Bis-(2,2-Dinitropropyl) Formal without Diphenyl Amine Stablizer

1000 mg/kg

Observation	Interim Death Incidence		Terminal Necropsy Incidence	
	M	F	M	F
No visible lesions	-	2	5	3

1600 mg/kg

Observation	Interim Death Incidence		Terminal Necropsy Incidence	
	M	F	M	F
No visible lesions	-	-	5	5

2500 mg/kg

Observation	Interim Death Incidence		Terminal Necropsy Incidence	
	M	F	M	F
No visible lesions	-	2	5	3

-: Not applicable

Table IV (continued)

Necropsy Observations (Incidence Values) of Five Unicharge Propellants in the Acute Exposure Oral Toxicity Study in Mice (14 Day)

PH 403-US-001,002-91

Bis-(2,2-Dinitropropyl) Formal without Diphenyl Amine Stablizer

4000 mg/kg

Observation	Interim Death Incidence		Terminal Necropsy Incidence	
	M	F	M	F
No visible lesions	2	1	3	4

5000 mg/kg

Observation	Interim Death Incidence		Terminal Necropsy Incidence	
	M	F	M	F
No visible lesions	3	3	1	-
Intestines				
distended	1	0	0	-
fluid-filled red	0	2	0	-

-: Not applicable

QUALITY ASSURANCE UNIT STATEMENT

Study Nos.: PH 403-US-001-91
PH 403-US-002-91

Study Director: Victor T. Mallory, B.S., RLAT

The Quality Assurance Unit conducted the inspections listed below and reported the results to the study director and to management on the dates indicated.

The following inspections were performed:

Interval	Date
In Life Phase	October 30, 1991
	October 30, 1991
Necropsy Phase	November 26, 1991
	November 26, 1991
Reporting Phase	January 29, 1992

Date QAU Report Issued

To Study Director	To Management
January 29, 1992	January 29, 1992

Leslie J. Rinnell
Quality Assurance

May 29, 1992
Date

COMPLIANCE STATEMENT

This study was conducted in compliance with the Principles of Good Laboratory Practices (GLP) as promulgated by the following regulatory agencies.

EPA as stated in the Federal Register, 40 CFR Parts 160 and 792.

Organization for Economic Co-operation and Development Guidelines for Testing Chemicals (OECD), ISBN 92-64 12221-4, adopted by the council at its 535th meeting on 12th May, 1981.

Study Nos.: PH 403-US-001-91
PH 403-US-002-91

To the best of my knowledge, this study was conducted in accordance with applicable Good Laboratory Practice regulations; there were no deviations from these regulations that impacted on study conclusions.

Study Director

Date May 29, 1993